

ABSTRACT

In the biosynthetic reaction system of caffeine, enzymes which catalyze these reactions respectively, and a method of composite utilization of genes encoding these enzymes, respectively are provided. A process for producing 7-methylxanthine, theobromine or caffeine which comprises methylation of xanthosine, ribose removal of 7-methylxanthosine, methylation of 7-methylxanthine, and/or methylation of theobromine *ex vivo*, in the presence of a combination of two or more of the enzymes a, c and d, and the cellular extract b. a: an enzyme which catalyzes methylation of xanthosine at the 7-position of the purine ring and has the amino acid sequence set out in SEQ ID NO: 1, b: a crude cellular extract obtained from *Escherichia coli* which catalyzes ribose removal of 7-methylxanthosine at the 9-position of the purine ring, c: an enzyme which catalyzes methylation of 7-methylxanthine at the 3-position of the purine ring and has the amino acid sequence set out in SEQ ID NO: 4, d: an enzyme which catalyzes methylation of theobromine at the 1-position of the purine ring and has the amino acid sequence set out in SEQ ID NO: 7.